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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/536,735	03/28/2000	Simone Gauch	QGN-009.2US	5502

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LEON R. YANKWICH
YANKWICH & ASSOCIATES
201 BROADWAY
CAMBRIDGE, MA 02139

EXAMINER	
SISSON, BRADLEY L	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/536,735	GAUCH ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-13,20,37-56,58-75,112-116 and 121-129* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-13,20,37-56,58-75,112-116 and 121-129* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 11 February 2004 has been entered.

Requirement for Information

2. Applicant and the assignee of this application are required under 37 CFR 1.105 to provide the following information that the examiner has determined is reasonably necessary to the examination of this application.

3. The instant application is a continuation-in-part of PCT/EP99/02664, filed 20 April 1999. Applicant is required to clearly indicate what material was added, and/or removed, from the instant application over that of the parent documents.

4. In response to this requirement, please provide a copy of each of the following items of art referred to in the instant disclosure at pages 30, 32, 33, 37, 43, 44, 45: Information relating to the sale, use, package instruction and formulation of RLT, RW1, RPE, AW, AL, AW1, and AW2 buffers from QIAGEN GmbH, Hilden, DE; and art referred to at page 46 as it relates to the sale, use, and formulation of QIAmp Mini-Spin Column from QIAGEN; and art referred to at

page 59 and 60 as it relates to the sale, use, package instruction and formulation of RNeasy-Kits from QIAGEN.

5. In response to this requirement, please provide the names of any products or services that have incorporated the claimed subject matter.

6. The fee and certification requirements of 37 CFR 1.97 are waived for those documents submitted in reply to this requirement. This waiver extends only to those documents within the scope of this requirement under 37 CFR 1.105 that are included in the applicant's first complete communication responding to this requirement. Any supplemental replies subsequent to the first communication responding to this requirement and any information disclosures beyond the scope of this requirement under 37 CFR 1.105 are subject to the fee and certification requirements of 37 CFR 1.97.

7. The applicant is reminded that the reply to this requirement must be made with candor and good faith under 37 CFR 1.56. Where the applicant does not have or cannot readily obtain an item of required information, a statement that the item is unknown or cannot be readily obtained will be accepted as a complete reply to the requirement for that item.

8. This requirement is an attachment of the enclosed Office action. A complete reply to the enclosed Office action must include a complete reply to this requirement. The time period for reply to this requirement coincides with the time period for reply to the enclosed Office action.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

> pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 9-13, 20, 37-56, 58-75, 112-116, and 121-129 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision of *Vas-Cath Inc. v. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

> This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 USC 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the "applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

For convenience, Claim 9, the only independent claim, is reproduced below.

9. (currently amended) A process for the isolation of nucleic acids from a sample comprising the following steps:

(a) applying at least one nucleic acid sample to a non-siliceous surface;

(b) immobilizing the nucleic acids of the nucleic acid sample on the non-siliceous surface in the presence of:

(i) a compound selected from the group consisting of a salt of a metal and/or ammonium cation with a mineral acid, a salt of a mono or polybasic or polyfunctional organic acid with an alkaline or alkaline-earth metal, a chaotropic agent, and combinations thereof, and

(ii) a hydroxy-functional compound of an aliphatic or acyclic saturated or unsaturated hydrocarbon, a phenol, or a polyphenol, wherein the nucleic acids are reversibly immobilized on the non-siliceous surface;

(c) releasing the immobilized nucleic acids from the non-siliceous surface with an elution agent, characterized in that the release takes place at a temperature T, whereby $10°C \geq T \geq T_{s,EM}$, and $T_{s,EM}$ equals the freezing point of the elution agent.

11. For purposes of examination, claim 9 has been interpreted as encompassing the isolation of nucleic acids from virtually any sample, wherein the sample cam comprise or consist of fecal matter, intact cells, crude oil, plant material, viruses, bacteria, as well as disrupted collections and suspensions of any of the aforementioned.

12. The "surface" has been interpreted as encompassing virtually any solid phase material that has at least one surface. The method of claim 9, and claims that depend therefrom, have been interpreted as encompassing the use of any of concentration of any of the identified compounds.

13. A review of the disclosure finds several examples having been presented. It is clear that applicant has been able to achieve isolation of specific nucleic acid samples that have undergone pretreatment such that the nucleic acids are free to bind to the support. It is also clear that the record support isolation of nucleic acids using commercially available spin columns, and

commercially available buffers, e.g., RLT, RW1, RPE, AW, AL, AW1, and AW2 buffers from QIAGEN GmbH, Hilden, DE. A review of the disclosure fails to find adequate written support for the isolation of any nucleic acid, e.g., mitochondrial DNA, though such is fairly encompassed by the claims. The specification has not been found to provide an adequate written description of how any nucleic acid, including monomers (specification at page 4, lines 10-17), when any concentration of a salt of a metal and/or ammonium cation with a mineral acid, a salt of a mono or polybasic or polyfunctional organic acid with an alkaline or alkaline-earth metal, a chaotropic agent, a hydroxy-functional compound of an aliphatic or acyclic saturated or unsaturated hydrocarbon, a phenol, or a polyphenol is used, either alone or in combination.

14. In accordance with claim 39, one is to apply "a predetermined quantity of washing buffer on the non-siliceous surface." It is noted that the predetermined quantity and its use are not required to achieve any particular end product, e.g., the removal of some or all of the contaminants. The specification does not provide an adequate written description of a method whereby any predetermined volume of wash buffer can be used and the method still result in the desired end product, i.e., isolated nucleic acids.

15. In accordance with claim 43, the claimed method is to be conducted by "an automatic device." A review of the disclosure fails to find an adequate written description of the physical features of such a device, much less an adequate written description of the algorithm used to operate same.

16. In accordance with claim 45, "a majority of nucleic acid isolations or reactions take place simultaneously." Such language fairly encompasses performing binding reactions, sequencing reactions, and cloning reactions in a simultaneous manner. A review of the disclosure fails to

provide an adequate written description as to how multiple and divergent methods are all to be performed in a "simultaneous" manner.

17. As noted above, claims 9, 13, 20,37-56, 58-75, 112-116, and 121-129 fairly encompass performing the elution step at virtually any temperature lower than 10°C. A review of the disclosure, however, fails to find an adequate written description of where any temperature lower than or equal to 10°C had been contemplated. The record does support, however, does support a lower limit of -5°C (see page 7).

18. In accordance with claim 56, one is to employ an alkanol. As noted at page 13 of the specification, isopropanol is especially preferred. The membrane used in he claimed method has been interpreted as encompassing virtually any pore size. A review of the disclosure, however, fails to locate an adequate written description of where any pore size can be used. In support of this position, attention is directed to page 20, lines 10-12, the pore size "must be greater than 0.2 μm" when nucleic acids have been precipitated by isopropanol.

19. In accordance with claim 72, "the membrane is coated with a hydrophobizing coating agent selected from the group of paraffins, waxes, metal soaps, optionally containing additives selected from the group of aluminum or zirconium salts, quaternary organic compounds, ureic derivates, lipid modified resins, silicones, zinc organic compounds and glutaric dialdehyde." Said claim 72 has been interpreted as fairly encompassing the application of any amount of said coating material. In accordance with page 5 lines 8-9, of the disclosure, "a surface is defined as any microporous separating layer." The application of paraffins, waxes, lipid modified resins, etc., could easily obliterate the requisite microporous nature of he membrane, effectively rendering it non-porous. A review of the disclosure fails to find an adequate written description

of how such membranes are made and ultimately used. Additionally, the specification does not reasonably suggest that applicant was in possession of the full genus of membranes and other "surfaces" encompassed by the claims.

20. It appears that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness. Obviousness, however, cannot be relied upon for satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

For the above reasons, and in the absence of convincing evidence to the contrary, claims 9-13, 20, 37-56, 58-75, 112-116, and 121-129 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

21. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

22. Claims 37 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 37 is confusing as to what constitutes a "top" surface when there is no sidedness to the surface, e.g., the surface is that of a granule (claim 114).

23. Claim 43 is confusing as to what constitutes "essentially the same." Said claim is further indefinite when there is in fact no passage, but rather, the support is simply granules suspended in solution.

Double Patenting

24. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

25. Claims 9-13, 20, 37-56, 58-75, 112-116, and 121-129 are provisionally rejected under the judicially created doctrine of double patenting over claims 77-80, 82, 84, 93-95, and 1221-126 of copending Application No. 10/300,111. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

26. The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: a process for isolating nucleic acids

27. Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending

application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claim Rejections - 35 USC § 103

28. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

29. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

30. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

31. Claims 9-13, 20, 37-42, 45-50, 54-56, 58-67, 69, 70, 73-75, 112-114, 121-123, 125-129 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,234,809 (Boom et al.) in view of Fluka (page 1412).

32. Boom et al., columns 3-4, 6, and 7 teach reversibly immobilizing nucleic acids (DNA and RNA) to a slit support. The solid support can be a membrane (nitrocellulose/cellulose acetate) as well as granular (latex particles). Column 7 teaches a "Lysis buffer L6*." Said lysis buffer comprises a chaotropic agent, GuSCN, as well as potassium iodide, TRITIN X-100.

33. Fluka defines TRITON X-100 as polyethylene glycol tert-octylphenyl ether. This meets the limitation of the lysis buffer further comprising "a hydroxy-functional compound of an aliphatic or acyclic saturated or unsaturated hydrocarbon, a phenol, or a polyphenol."

34. Boom et al., column 7, disclose TE buffer, which was used to elute the nucleic acid.

35. Boom et al., column 13, teach simultaneous isolation of DNA and ssRNA.

36. Boom et al., column 14, teach isolation of DNA with multiple chaotropic agents.

37. Boom et al., column 15, disclose performing enzymatic steps on the isolated nucleic acid.

38. Neither Boom et al., nor Fluka disclose the claimed temperature range of eluting the reversibly immobilized nucleic acids at a temperature at or below 10°C.

The aspect of performing the disclosed method at or below 10°C is considered to be the result of routine optimization, as is the selection of concentrations of components of the various solutions and buffers, e.g., chaotropic agents, and as such, does not impart non-obviousness to the claimed invention. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

> Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however,

> changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In re Dreyfus, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; In re Waite et al., 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In re Swenson et al., 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; In re Scherl, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In re Sola, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; In re Normann et al., 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; In re Irmscher, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Swain et al., 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; Minnesota Mining and Mfg. Co. v. Coe, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; Allen et al. v. Coe, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

In view of the totality of the prior art of record, and in the absence of convincing evidence to the contrary, it would have been obvious to one of ordinary skill in the art, through routine optimization, to determine the appropriate concentrations and temperatures at which various nucleic acid can be isolated from any source. In view of the great interest in the area of technology t which nucleic acid chemistries belong, and the detailed teachings found in the prior art, the ordinary artisan would have been both well motivated and would have also had a most reasonably expectation of success. Accordingly, claims 9-13, 20, 37-42, 45-50, 54-56, 58-67, 69, 70, 73-75, 112-114, 121-123, 125-129 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,234,809 (Boom et al.) in view of Fluka (page 1412).

Conclusion

39. This Office action has an attached requirement for information under 37 CFR 1.105. A complete reply to this Office action must include a complete reply to the attached requirement

for information. The time period for reply to the attached requirement coincides with the time period for reply to this Office action.

40. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

41. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

42. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
08 March 2004

Gary Benzion

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600